UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,378	11/09/2001	Jeffrey T. Blue	20455P	8714

210 7590 03/15/2004

MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,378	BLUE, JEFFREY T.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *9-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-8* is/are rejected.

7)☒ Claim(s) *1-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/09/01, 03/14/03, 12/08/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: PTO-90C & Notice to Comply

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Applicant's response dated December 08, 2003 is acknowledged.

2. The traversal is on the ground(s) that Claims 1-17 meet the criteria set out in PCT Article 3342-44), because the prior art does not teach or fairly suggest a method for assaying the virulence of a particular virus by the employment and subsequent measurement of caspase 3 activity. This is found persuasive, however, the inventions continue to lack unity. The invention of Group I and Group II differs in active method steps. The active method steps of Group I include the contacting of cells with virus and measuring caspase 3 activity. The active method steps in Group II includes infecting cells with a formulation (A), contacting a different set of cells with a virus with a formulation (B), and measuring caspase 3 activity for each sets relating to the formulation (A and B). The method steps recited in the latter Group are not required in Group I. Thus, due to this difference in active method steps, the inventions lack unity. Further, it is noted that claims 9-17 should have been deemed unsearchable since claim 9 lacks antecedent basis for "virus".

The requirement is still deemed proper and is therefore made FINAL.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR

1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Nucleotide and/or amino acid sequences as used in § § 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. It appears that the claims in the instant application are in reference to four or more amino acid sequence, see claim 3.

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Objections

3. Claims 1-8 are objected to because of the following informalities:

For claims 1-3 and 6-8:The claims recitation of step (a) and/or step (b) is not consistent with the delimiter used in Claim 1. Claim 1 recites the use of only a closed/right parenthesis. Appropriate correction is required.

For claims 1-8 are directed to a method of assaying the potency and stability of a virus, however, step b) of the claims do not include the determination of a virus's

potency. As the claims are written, it only fulfills one aspect of the claimed invention, the measurement of caspase 3 activity as an indication of viral stability.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are rendered indefinite because it is unclear what the claimed method steps measure. The preamble of the claimed method recites viral potency and stability, yet the conclusion of the method steps do not refer back to the preamble. As it is written, the claimed method is only directed to the measurement of caspase 3 activity as an indicator of viral stability. To obviate this rejection, Applicant should recite "potency and stability" in the last method of the claims.

Claim 7 is indefinite because of the recitation of "two or more time intervals". It is unclear what is intended by "two or more time intervals". The recitation of "two or more time intervals", when used in full context with the claims can mean one of several things. The first interpretation that can be extracted from the recitation is that step a) is performed at time X and step b) is performed at time Y, wherein time Y is later than time X. The second meaning that can be inferred from the recitation is that step a) is performed at two X times, and step B is performed at only one Y time. The third

possible meaning that can be derived form the recitation is that both steps a) and b) are completed at time Y and repeated at time X, meaning that the method is repeated in the same sequence at a later time.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

7. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The nature of the claimed invention is drawn to the measurement of caspase 3 activity to determine the potency and stability of a virus. The breadth of the claims encompasses any virus and cells that are susceptible to caspase 3 induction.

However, the specification has not taught one of ordinary skill how to use the claimed invention. The specification does not contain any guidance on how the detection of caspase 3 activity of a virus on cells can be used as an indicator of viral potency and stability. The only guidance that Applicant has shown, which is demonstrated in the working examples, is that Caspase 3 activity is detected for rubella, measles, and mumps viruses in cultured Vero and RK-13 cells. However, again, it does not teach how this information can be use as an indicator of viral potency and stability.

In addition, the specification also teaches that caspase 3 activity follows a hyperbolic curve, wherein the activity reaches a peak climax and begins a downward fall thereafter; see Figure 1a and 1b. It is noted that this curve shown in Figures 2a and 2b are only representative of caspsase-3 activity at a time where the activity is on the positive incline. Thus, using this data presented in the figures provided, one of ordinary skill in the art can conclude that one can monitor caspase 3 activity over time. However, it still does not teach how this can be used to conclude on the potency and stability of viruses on cells.

Further, while the specification is not enabling for claimed invention, the claimed invention is also not enabled by the prior art. The prior art teach that hepatitis B virus HBx protein (Gottlob et al.), herpesvirus saimir (HVS) and other lymphotropic herpesviruses (Derfuss et al.), and EBV and BCL virus (Foghsgaard et al.) inhibit caspase 3 activity. However, the measurement of caspase-3 activity does not provide insight on the potency and stability of the viruses on the cells--yet the breadth of the claims encompasses any viruses. Further, the prior art also teaches that cells undergo apoptosis in a responses to a wide range of environmental cues (Villa et al.). Therefore, monitoring of cell death as it relates to caspsa-3 activity and viral infectivity does not provide any indication of viral stability and potency. From the teachings of the prior art, it is concluded that the level of predictability in the art for the instantly claimed invention is low because there is no nexus between viral potency and stability, and caspase 3 activity.

For these reasons, it is determined that an undue quantity of experimentation would be required of the skilled artisan, with relatively high skill in the art, to make and use the invention.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wrigtht*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E.Le

Emily Le

Shanon Foley

Shanon Foley
Patent Examiner, AU 1648

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER
	20040223

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This Application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirement of 37 C.F.R. §§ 1.821-1.825 for the reasons(s) set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/OR amino Acid Sequence Disclosures.

APPLICANT IS GIVEN 30 days FROM The DATE OF THIS LETTER WITHIN Which TO COMPLY WITH The SEQUENCE RULES, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.82(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond six month statutory period. Direct the response to the undersigned. Applicant is required to return a copy of the attached Notice to Comply with the response.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Emily Le
Emily Le

Shanon Foley
Patent Examiner, 1600

Notice to Comply	Application No.	Applicant(s)	
	10/030,378	Jeffrey Blue	
	Examiner	Art Unit	
	Emily Le	1648	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

X 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

X 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

X 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

X 7. Other: Applicant must append SEQ ID NOs to all mentions of specific sequences. Appropriate correction is required.

Applicant Must Provide:

X An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

X An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

X A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY